

IN THE SPECIFICATION:

Please amend the specification as follows.

On page 1, please replace the paragraph immediately below the title with the following paragraph:

M2

This is a continuation in part of International application Serial No. PCT/US95/05688, filed May 1, 1995, which is a continuation in part of U.S. application Serial No. 08/236,208, filed May 2, 1994, which issued as U.S. Patent No. 6,074,642 on June 13, 2000. International application Serial No. PCT/US95/05688 was published in English under PCT Article 21(2) on November 9, 1995 as WO 95/29697.

Please replace the paragraph at page 38, lines 1-22, with the following paragraph:

M2

Useful expression vectors for bacterial use can comprise a selectable marker and bacterial origin of replication derived from commercially available plasmids comprising genetic elements of the well-known cloning vector pBR322 (American Type Culture Collection -"ATCC"-, 10801 University Boulevard, Manassas, VA 20110-2209, United States of America; ATCC Accession No. 37017). These pBR322 "backbone sections," or functionally equivalent sequences, are combined with an appropriate promoter and the structural gene to be expressed. Promoters commonly used in recombinant microbial expression vectors include, but are not limited to, the lactose promoter system (Chang, et al., Nature 275:615), the tryptophan (trp) promoter (Goeddel, et al., 1980, Gene Expression Technology, Volume 185. Academic Press, Inc., San Diego, CA) and the tac promoter, or a fusion between the tac and trp promoters referred to as the trc promoter (Maniatis, 1982, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, Cold Spring

26

M

Harbor, NY). Particularly preferred promoters include the T7 promoter, which is used in conjunction with host cell expression of a T7 RNA polymerase (see Studier et al. 1990, Meth. Enzymol. 185:60-89), and the trc promoter, which is found in several commercially available vectors, as described below.

M³
Cont.

Please replace the paragraph at page 52, lines 9-11, with the following paragraph:

72. An isolated oligopeptide comprising an amino acid sequence corresponding to amino acid 8 through amino acid 12 of SEQ ID NO:1, i.e., Lys Ser Ser Lys Cys, or in single letter notation, KSSKC.

M⁴

Please replace the paragraph at page 60, lines 22-34, with the following paragraph:

At each time point an aliquot of blood was taken, and subaliquots were centrifuged to remove all cells and the remaining plasma diluted 1:1 in QUIDEL sample preservation solution (Quidel Corporation, San Diego, CA) and stored at -80°C for subsequent evaluation of soluble C5b-9 (sC5b-9) generation. Diluted subaliquots of plasma were also frozen for evaluation of C3a generation (see Example 5, below). Undiluted subaliquots of plasma were frozen at -80°C for analysis in hemolytic assays to evaluate the pharmacokinetics of the effects of the anti-C5 antibodies on the cell lysing ability of complement present in the blood (see Example 6, below). These experiments are also discussed in copending US patent application Serial No. 08/217,391, filed March 23, 1994, now US patent No. 5,853,722.

M⁵

200

M

Please replace the paragraph at page 62, lines 11-18, with the following paragraph:

M
The plasma samples that had previously been diluted in QUIDEL sample preservation solution and frozen (see Example 4) were assayed for the presence of C3a by using the QUIDEL C3A EIA kit (Quidel Corporation, San Diego, CA) according to the manufacturer's specifications. Concentrations of C3a in the samples is expressed as ng/well as determined by comparison to a standard curve generated from samples containing known amounts of human C3a.

Please replace the paragraph at page 65, lines 3-26, with the following paragraph:

M
A 50 μ L aliquot of a 2 μ g/mL solution of C5 (Quidel Corporation, San Diego, CA) in sodium carbonate /bicarbonate buffer, pH 9.5, was incubated overnight at 4°C in each test well of a 96 well plate (NUNC-IMMUNO F96 POLYSORP, A/S Nunc, Roskilde, Denmark). The wells were then subjected to a wash step. (Each wash step consisted of three washes with TBST.) Next, test wells were blocked with 200 μ L of blocking solution, 1% BSA in TBS (BSA/TBS) for 1 hour at 37°C. After an additional wash step, a 50 μ L aliquot of hybridoma supernatant was incubated in each test well for 1 hour at 37°C with a subsequent wash step. As a secondary (detection) antibody, 50 μ L of a 1:2000 dilution of horseradish peroxidase (HRP) conjugated goat anti-mouse IgG in BSA/TBS, was incubated in each test well for 1 hour at 37°C, followed by a wash step. Following the manufacturer's procedures, 10 mg of O-phenylenediamine (Sigma Chemical Company, St. Louis, MO, Catalog No. P-8287) was dissolved in 25 mLs of phosphate-citrate

μ
cont

buffer (Sigma Chemical Company, St. Louis, MO, Catalog No. P-4922), and 50 μ L of this substrate solution was added to each well to allow detection of peroxidase activity. Finally, to stop the peroxidase detection reaction, a 50 μ L aliquot of 3N hydrochloric acid was added to each well. The presence of antibodies reactive with C5 in the hybridoma supernatants was read out by a spectrophotometric OD determination at 490 nm.

M 8

Please replace the paragraph at page 66, line 36 - page 67, line 6, with the following paragraph:

Hybridoma 5G1.1 was deposited with the American Type Culture Collection, 10801 University Boulevard, Manassas, VA 20110-2209, United States of America, on April 27, 1994, and has been assigned the designation HB-11625. This deposit were made under the Budapest Treaty on the International Recognition of the Deposit of Micro-organisms for the Purposes of Patent Procedure (1977).

M 9

Please replace the paragraph at page 81, lines 2-11, with the following paragraph:

The extract supernatant was diluted 10-fold with 20 mM Tris-HCL pH 9.0, 7 M urea, 50 μ M cupric sulfate and allowed to stir for at least 16 hours at 4°C to refold the scFv. After addition of BIOCRYL BPA-1000 (TosoHaas, Montgomeryville, PA) as a flocculating agent at 3 μ l per ml, the sample was centrifuged at 15,000 x g for 10 minutes to remove insoluble material. The refolding mixture was exchanged into 20 mM Tris, pH 9.0, 1mM EDTA by diafiltration and concentrated by ultrafiltration using a stirred cell fitted with a YM10 membrane (Amicon, Beverly, MA).

208

M

Please replace the paragraph at page 81, line 30 - page, 82, line 7, with the following paragraph:

In the initial experiments, the properly refolded scFv was then separated from aggregated material and contaminating proteins by anion exchange chromatography using Q SEPHAROSE FAST FLOW (Pharmacia, Piscataway, NJ). Bound scFv was eluted with 20 mM Tris-HCL pH 9.0, 1 mM EDTA containing a linear NaCl gradient (0 to 0.5 M). The fractions containing the scFv were combined, concentrated by ultrafiltration using a stirred cell fitted with a YM10 membrane, and applied to a SEPHACRYL S200 HR 26/100 gel filtration column (Pharmacia) equilibrated in 20 mM Tris-HCL pH 9.0, 1 mM EDTA, 150 mM NaCl. Fractions containing the scFv were combined, exchanged into phosphate-buffered saline by diafiltration, concentrated by ultrafiltration, filtered through a 0.22 μ m MILLEX-GV filter (Millipore, Bedford, MA), and stored at 4°C.

Please replace the paragraph at page 82, lines 21-28, with the following paragraph:

Frozen bacterial cell paste was thawed and resuspended in 2.5 ml of 1 mM EDTA (pH 5) per gram of cell paste. This suspension of cells was lysed by passage through a MICROFLUIDIZER (Microfluidics) with the interaction chamber in line and a backpressure of approximately 18000 psi. The cell lysate was then centrifuged at 10,000 rpm in a JA-10 centrifuge rotor at 4°C for 15 min. The supernatant was decanted and discarded.

Please replace the paragraph at page 83, lines 24-33, with the following paragraph:

The diluted retentate was then loaded at 4°C onto a SP SEPHAROSE FF column (Pharmacia) equilibrated in 0.7 M urea, 1

M12
Cont

mM EDTA, 10 mM NaCl, 20 mM sodium acetate, pH 5.0, at a linear flowrate of 5 cm/min. Bed height was equal to or greater than 3.5 cm. Following loading the column was washed with 40 column volumes (CV) of equilibration buffer. The column was then washed with 20 CV of 20 mM sodium acetate, pH 5.0, 1 mM EDTA. The bound scFv was then eluted using 20 mM sodium citrate, pH 5.8, 1 mM EDTA. A single peak was collected in approximately 4 column volumes.

Please replace the paragraphs at page 83, line 34 - page 84, line 12, with the following paragraphs:

M13

The SP SEPHAROSE eluate was then adjusted to 20 mM Tris-HCL by addition of 1 M Tris-HCL, pH 8. The pH of the sample was adjusted to 8.0 by addition of 1 N NaOH. This sample was loaded onto a Q SEPHAROSE FF column (Pharmacia) equilibrated in 20 mM Tris-HCL, pH 8.0, 1 mM EDTA at room temperature at a flowrate of 5 cm/min. The flow through fraction containing the scFv was collected.

The Q SEPHAROSE flow through fraction was then adjusted to 150 mM NaCl and concentrated to 10 mg of scFv per ml using a 10 kDa cutoff ultrafiltration membrane. This concentrated sample was then loaded onto a SEPHACRYL S200 column equilibrated in phosphate buffered saline, pH 7.4 and eluted at 0.4 cm/min. The fractions were analyzed by SDS-PAGE and silver staining. Peak fractions were combined after discarding the front and back shoulder fractions that contained the majority of contaminants.

Please replace the paragraph at page 85, line 28 - page 86, line 9, with the following paragraph:

M14

The filters were incubated twice for 30 minutes each in blocking solution (500 mM NaCl, 5 mM Tris pH 7.4, 10% (v/v) nonfat